

Crohn's disease of the duodenum

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SUMMARY Crohn's disease of the duodenum is uncommon, occurring in approximately 2% of patients with Crohn's disease. Approximately 165 cases have been reported in small series in the literature. Our report includes 36 patients, most of whom had symptoms of duodenal disease co-incident with or after obvious disease elsewhere in the gastrointestinal tract, although occasionally duodenal disease developed first and rarely disease was confined to the duodenum. Upper abdominal pain and symptoms of gastroduodenal obstruction are the commonest patterns of presentation. Significant weight loss is common, and occasionally major upper gastrointestinal bleeding occurs. The commonest pattern of involvement was contiguous disease of the proximal duodenum and distal stomach. Endoscopically, diffuse granularity, nodularity, and ulceration are seen accompanied by lack of distensibility of the involved area. Granulomas are rarely found in endoscopic biopsies. A bypass procedure was carried out on 18 patients, 15 of whom continue to be free of symptoms with an average follow-up of 6.6 years. When symptoms of obstruction dictate, operative bypass is accompanied by favourable long-term results in the large majority of patients.

Crohn's disease most commonly involves the terminal ileum or colon but it may occur in any part of the alimentary tract from the mouth to the anus (Bishop *et al.*, 1972; Fedotin *et al.*, 1974). Involvement of the duodenum is uncommon but is being recognised with increasing frequency. In a review of the world literature in 1965, Edwards *et al.* (1965) revealed that only 48 cases had been reported. Since then, an additional 76 cases have been cited in a review by Paget *et al.* (1972). Further scattered reports have appeared (Bagby *et al.*, 1972; Farmer *et al.*, 1972; Roseman, 1972; Sanders and Schimmel, 1972; Haggitt and Meissner, 1973; Kim *et al.*, 1973; Thompson *et al.*, 1975) increasing the total number to approximately 165 cases.

We have encountered 36 patients with Crohn's disease involving the duodenum over a 20 year period. The clinical, radiological, endoscopic, and pathological features of this uncommon entity and the results of medical and surgical management are reported.

Methods

PATIENTS

All patients with a diagnosis of Crohn's disease of

the duodenum seen between 1955 and 1974 were included in our review. Diagnosis was established by one of two criteria: the histological finding of non-caseating granulomatous inflammation of the duodenum with or without obvious Crohn's disease elsewhere in the intestinal tract and without evidence of any systemic granulomatous disease, or Crohn's disease of the small or large bowel and a radiological finding of diffuse inflammatory change in the duodenum consistent with Crohn's disease.

Clinical features

Twenty-five men and 11 women were included in the group of patients studied. Age at onset of Crohn's disease varied from 5 to 59 years (mean, 27 years), and age at onset of duodenal Crohn's disease ranged from 5 to 67 years (mean, 30 years).

Of these patients, in 19 the onset of duodenal disease appeared to coincide with the onset of disease in other parts of the gastrointestinal tract; 11 patients had obvious disease elsewhere of four to 40 years' duration (mean, 10 years) before duodenal disease developed. In six patients disease was initially confined to the duodenum with or without involvement of the gastric antrum. In one of these six patients, terminal ileitis developed four years later. In another, widespread jejunal disease in continuity with disease in the duodenum developed seven years later, and, in a third patient, severe diffuse gastric Crohn's disease requiring total gastrectomy occurred 20 years later. In the other three patients the disease remained confined to the

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duodenum throughout its course, although all three had histological involvement of the gastric antrum.

Of the 32 patients who had Crohn's disease elsewhere in their gastrointestinal tract (excluding stomach), one had oesophageal disease, five had disease in the proximal small intestine, 16 had disease in the terminal ileum, seven had colonic disease, and three had widespread disease throughout the small and large intestine.

Symptoms

The symptoms of Crohn's disease of the duodenum are listed in the Table. Epigastric pain was by far

Table Clinical symptoms 36 patients

	Number	Percent
Pain	35	97
Nausea	27	75
Vomiting	20	56
Weight loss (> 4.5 kg)	22	61
Melaena	5	14
Fever	2	6

the commonest symptom; most often it was postprandial and accompanied by nausea and sometimes vomiting. Vomiting usually offered relief of pain. Some patients had pain suggestive of duodenal ulcer pain in that it was relieved by food or antacids, although it was not usually episodic. In the majority of patients, symptoms reflected the obstructive nature of the lesion. Significant weight loss was common. Major upper gastrointestinal bleeding, presenting as haematemesis or melaena, occurred in five patients.

Radiology

Radiologically, three patterns of disease were noted in the duodenum. The first and commonest was contiguous involvement of the gastric antrum and proximal duodenum. Of the 36 patients, 20 had this pattern of involvement radiologically (seven others had histological evidence of gastroduodenal disease with radiological changes confined to the duodenum). A second pattern, seen in six patients, was involvement of an isolated segment of the descending duodenum. The third pattern was involvement of the distal duodenum. Three patients had this pattern, all of whom had contiguous involvement of at least a short segment of proximal jejunum.

The earliest radiological features, regardless of the site of disease, were irregular thickening, oedema, and a cobblestone pattern of the mucosa (Figure, A). As the disease progresses, stenosis becomes a prominent finding (Figure, B). Eventually, stenosis becomes severe and a string sign develops (Figure, C).

Fissures and pseudodiverticula were seen occasion-

ally. Reflux of barium into the common bile duct and pancreatic duct occurred in one patient. In patients with gastroduodenal involvement, progressive stenosis of the pyloric area may produce a pseudo-Billroth I appearance, in which the identity of the pylorus becomes entirely obscured (Figure, D).

Endoscopy

Endoscopic examination was carried out on 17 patients, and biopsies were obtained. The mucosa of the involved antrum and duodenum had a diffusely granular appearance with some nodularity and varying degrees of superficial ulceration. Linear ulcers were seen at times, and stiffness and lack of distensibility of the involved area were noted. Varying degrees of stenosis were encountered, and, in some, the involved areas were markedly rigid with stricture formation. The endoscope could not always traverse the pyloric canal or duodenum because of the stenosis.

Pathological features

At the time of operation, the appearance of a thickened, indurated, and oedematous duodenum suggests the diagnosis of Crohn's disease. Enlarged mesenteric lymph nodes and thickening and oedema of the mesentery may be present. When the mucosa is exposed by duodenotomy, it appears oedematous with thickened folds and has a granular surface. Mucosal ulcerations are sometimes obvious and may be superficial or deep (Haggitt and Meissner, 1973). Histologically, there is chronic inflammation and fibrosis involving the entire duodenal wall, and noncaseating granulomas may be present in any layer of the wall or in the regional lymph nodes. The histological changes are identical with those seen in Crohn's disease elsewhere in the gastrointestinal tract.

Of our patients 28 had histological diagnoses either at the time of operation or by endoscopic or capsule biopsy. Twelve patients had all histological features of Crohn's disease, including granulomas. In 16 patients, no granulomas were identified, but chronic inflammation and fibrosis of the duodenal wall, consistent with the diagnosis of Crohn's disease, were seen. Granulomas were not demonstrated in any of the 17 patients who had endoscopic biopsies. A gastric specimen from one of the three patients who had a capsule biopsy revealed granulomas.

Treatment

Of the 36 patients, 20 were operated on for obstruction of the pylorus or duodenum. Of these, 18 patients had a bypass procedure (gastroenterostomy and vagotomy, six; gastroenterostomy, six; Billroth

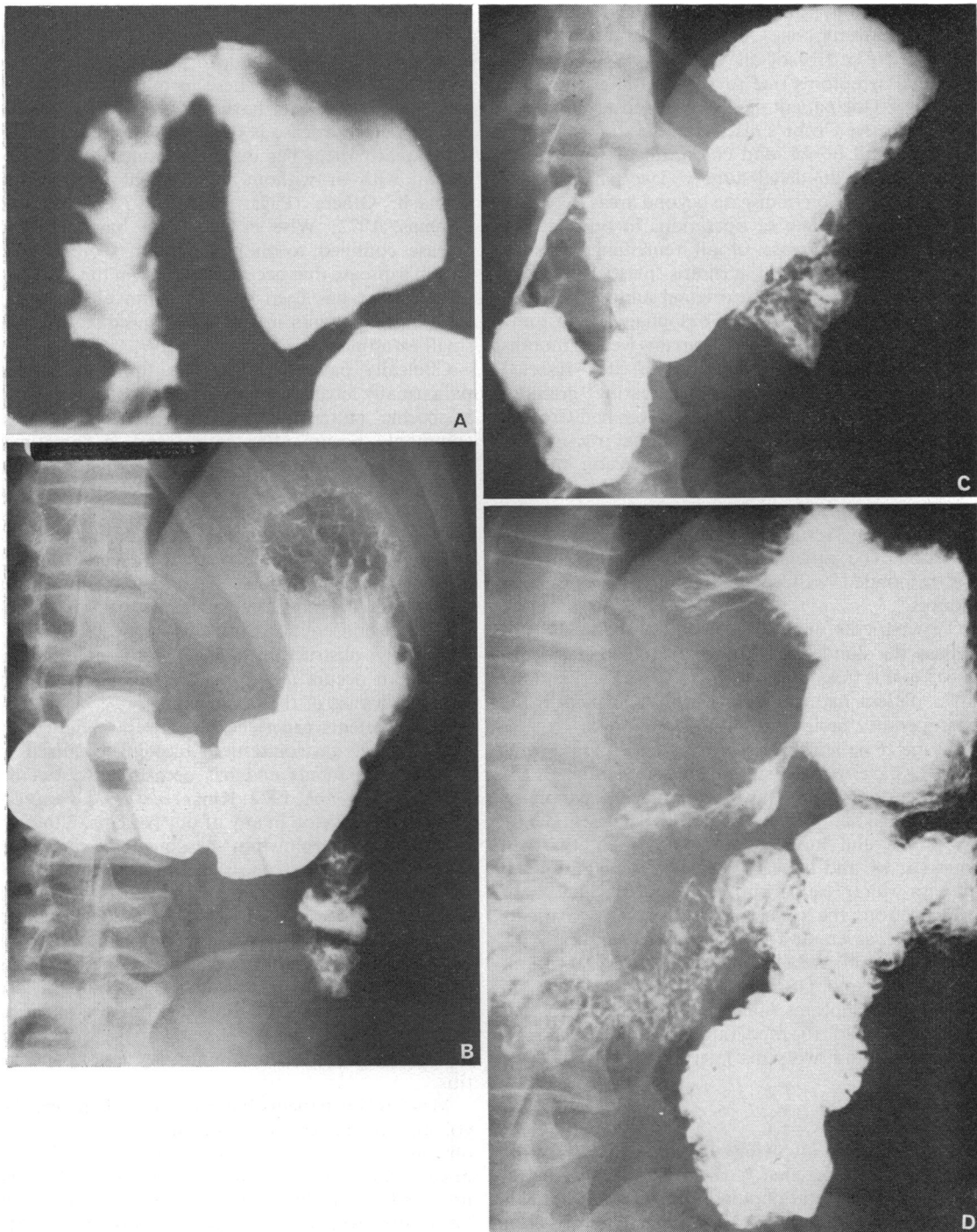


Figure *A: early radiological changes of oedema and cobblestone pattern. B: stenosis and deformity of the gastric antrum and proximal duodenum. C: marked stenosis with string sign. D: obliteration of the pylorus: 'pseudo-Billroth I.'*

II and vagotomy, three; Billroth II, two; and duodenojejunostomy, one). Of these 18 patients, 15 continue to be free of all significant upper gastrointestinal symptoms one to 19 years later (average, 6.6 years). One patient died six years after operation from extensive Crohn's disease of the stomach, duodenum, small bowel, and colon, all of which were present before duodenal surgery. Two patients have had local extension of disease beyond areas that were involved at the time of operation. In one patient, severe Crohn's disease of all remaining stomach developed, resulting in a linitis plastica type of lesion. Four years after the original subtotal gastrectomy, total gastrectomy with oesophagojejunostomy was required, and the patient remains well 18 months later. Histological examination of the resected stomach revealed diffuse, noncaseating granulomatous disease. This patient has never had Crohn's disease elsewhere in the gastrointestinal tract. In the second patient, widespread local extension into the distal half of the stomach and into the proximal jejunum developed four years after gastroenterostomy and vagotomy, resulting in partial small bowel obstruction. The patient was treated with steroids and has responded well to treatment for the past 18 months.

Two patients underwent operations that did not bypass the duodenum. One patient had a pyloroplasty and is free of symptoms 11 years later, and the other patient had a duodenectomy and died in the postoperative period.

Of the 16 patients who were treated without operation, 12 have received steroids intermittently. Of the 12 patients, four now have no significant symptoms one, two, six, and six years later, five have moderate symptoms and mild to moderate disability (two, four, six, 14, and 14 years later) and three have died, all with widespread Crohn's disease which had been present from the onset of disease. These patients died three, seven, and 19 years after operation.

Four patients were treated conservatively without steroid therapy. Of these patients, two have no significant symptoms (nine and 15 years later), and two have mild to moderate symptoms and disability (one and two years later).

Discussion

Crohn's disease involving the duodenum is quite rare. The 36 cases that have been presented represent 2% of the total population of the new patients with Crohn's disease we saw during the 20 year period. Others (Van Patter *et al.*, 1954; Jones *et al.*, 1966; Fielding *et al.*, 1970; Legge *et al.*, 1970) have reported the incidence to be from 0.5% to 4%. Age and sex distribution are not unlike those for Crohn's

disease located elsewhere.

In most patients, symptoms of duodenal disease develop at the same time as or after the appearance of obvious disease elsewhere in the gastrointestinal tract. A few patients have symptoms of duodenal disease before disease is detected elsewhere, and an occasional patient has disease confined to the duodenum with or without involvement of the distal stomach. Others (Paget *et al.*, 1972; Silva and Thomas, 1972; Wise *et al.*, 1971) have reported disease confined to the duodenum. Concomitant Crohn's disease that occurs elsewhere in the gastrointestinal tract has been reported from all sites, but most of the patients in our series had disease in the small intestine.

Clinically, patients present with upper abdominal pain usually localised to the epigastrium and without a specific pattern of radiation. The pain most commonly occurs after eating and is sometimes accompanied by nausea. Symptoms of high intestinal obstruction may or may not be present. In some patients, the pain has characteristics suggestive of duodenal ulcer in that relief is obtained with antacids or food. In some cases it is difficult to differentiate duodenal Crohn's from peptic ulcer. This differential diagnosis must depend upon radiological, endoscopic, and histological findings. Eventually, obstruction of the pylorus or proximal duodenum occurs in the majority of patients with Crohn's disease of the duodenum.

Most patients experience significant weight loss. Major upper gastrointestinal bleeding occurred in five of our patients and has occasionally been reported (Paget *et al.*, 1972; Kim *et al.*, 1973). Pancreatitis did not develop in any of our patients, although free reflux of barium into the pancreatic and common bile ducts was seen in one patient. Legge *et al.* (1971) reported evidence of pancreatitis in four of 11 patients, three of whom had reflux of barium into the pancreatic duct and another had reflux of barium into the biliary tract. Three of these patients had an accompanying rise in the serum amylase level. The similarity of the symptoms of pancreatitis to those of Crohn's disease of the duodenum makes it difficult to detect minor degrees of pancreatitis.

Most of our patients had radiological changes involving the proximal duodenum. The pylorus is obviously not a barrier to extension of Crohn's disease; all of our patients with involvement of the proximal duodenum also had involvement of the distal stomach, although this was not always apparent radiologically. A few patients had involvement of an isolated segment of the middle part of the duodenum, and a few had involvement of the distal duodenum with contiguous involvement of the

proximal jejunum. Characteristically, radiological changes included evidence of diffuse inflammatory change, oedema, and ulceration, with eventual stenosis or obstruction (Durrance, 1962; Roberts and Hamilton, 1966; Cohen, 1967; Nelson, 1969; Fielding *et al.*, 1970; Bagby *et al.*, 1972). None of our patients had spontaneous perforation or fistula from the duodenum, and these complications are not reported in the literature; however, an occasional patient has had a fistula after operation on the duodenum (Fielding *et al.*, 1970; Hermos *et al.*, 1970).

Relatively little information has been reported in the literature regarding the endoscopic appearance of Crohn's disease of the duodenum. Roseman (1972) reported a single case in which enlarged, rigid prepyloric folds were noted as well as similar large, stiffened folds in the duodenum, but no ulcerations were seen. Biopsy of the duodenal mucosa revealed nonspecific inflammation and a noncaseating granuloma.

Danzi *et al.* (1976) described 14 patients with Crohn's disease of the stomach or duodenum, three with duodenal involvement alone. Endoscopic findings revealed diffuse nodularity and granularity with superficial erosions and ulcerations. Thickening of the antral and duodenal folds was noted with some degree of stenosis. Two of nine endoscopic biopsies demonstrated granulomatous inflammation; the others were nonspecific.

In our patients, diffuse granularity, nodularity, and stiffening of the folds were universally seen. The ulcerations present in most instances varied from superficial erosions to larger ulcerations. The wall of the gastric antrum and duodenum demonstrated lack of distensibility with poor contractions and varying degrees of stenosis. At times stenosis prevented passage of the endoscope through the distal antrum, pylorus, or proximal duodenum.

Unfortunately, biopsy specimens obtained by endoscopic means are small and are limited to the mucosa. This poses a problem in the histological confirmation of Crohn's disease of the duodenum. We were unable to find granulomas in any of the 17 patients in our series who had endoscopic biopsies. Of the three patients who had capsule biopsies, granulomas were identified in one. Haggitt and Meissner (1973) reported that granulomas are commoner in the mucosa in Crohn's disease of the duodenum than in Crohn's disease lower in the gastrointestinal tract. We have been disappointed, however, by our inability to demonstrate granulomas in endoscopic biopsies in patients who were operated on subsequently and in whom granulomas were present in the deeper layers of the gastric or duodenal wall. Hermos *et al.* (1970) found granulomas in two patients who had biopsies with a biopsy

capsule. Multiple biopsies were performed on both patients, and results were entirely normal in some of these examinations. Mucosal involvement may be patchy, and the finding of nonspecific inflammation without granulomas, or even a normal biopsy, does not exclude the presence of Crohn's disease.

Medical treatment should be the treatment of choice for all patients with nonobstructing Crohn's disease of the duodenum and is similar to that of Crohn's disease elsewhere in the gastrointestinal tract (Nugent, 1975). If obstruction develops, bypass surgery is indicated, and our experience and that of others (Fielding *et al.*, 1970; Farmer *et al.*, 1972) suggests that it is accompanied by excellent long-term relief of the duodenal symptoms. As long as the duodenum that is involved is bypassed, the exact type of procedure does not seem important.

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Addendum

Since this manuscript was originally written, we have seen an additional eight patients with duodenal Crohn's disease. Seven have had endoscopic biopsies, and in four granulomas were demonstrated. Three of these patients have had bypass operations (total of 18), and all three have had complete relief of upper gastrointestinal symptoms (18 of 21 in all).